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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/555,629	07/31/2001	Naoki Yamazaki	2520-0118P	1386

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EXAMINER	
BUNNER, BRIDGET E	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 04/19/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/555,629	YAMAZAKI ET AL.	
	Examiner	Art Unit	
	Bridget E. Bunner	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *05 January 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7* is/are pending in the application.

4a) Of the above claim(s) *1-5* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *6 and 7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-7* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/5/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments and/or Claims

The amendment of 05 January 2004 has been entered in full. Claims 6-7 are amended.

This application contains claims 1-5drawn to an invention nonelected with traverse in the paper of 02 April 2003. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 6-7 are under consideration in the instant application.

Withdrawn Objections and/or Rejections

1. The objection to the specification at pg 3-4 of the previous Office Action (03 July 2003) are *withdrawn* in view of the amended title (05 January 2004).

2. The objection to claims 6-7 at pg 4 of the previous Office Action (03 July 2003) is *withdrawn* in view of the amended claims (05 January 2004).

3. The rejections to claims 6 under 35 U.S.C. § 112, first paragraph, as set forth at pg 4-7 of the previous Office Action (03 July 2003) are *withdrawn in part* in view of the amended claim (05 January 2004). Please see section on 35 U.S.C. § 112, first paragraph below.

4. The rejections to claims 7 under 35 U.S.C. § 112, first paragraph, as set forth at pg 7-10 of the previous Office Action (03 July 2003) are *withdrawn in part* in view of the amended claim (05 January 2004). Please see section on 35 U.S.C. § 112, first paragraph below.

5. The rejections to claims 6-7 under 35 U.S.C. § 112, second paragraph, as set forth at pg 10-11 of the previous Office Action (03 July 2003) are *withdrawn in part* in view of the

amended claims (05 January 2004). Please see section on 35 U.S.C. § 112, second paragraph, below.

6. The rejection of claims 6-7 under 35 U.S.C. § 102(b) as set forth at pg 11 of the previous Office Action (03 July 2003) is *withdrawn* in view of the amended claims (05 January 2004). It is noted that the prior art does not teach continuous administration of HGF to patients suffering from renal failure or occlusive lesion of blood vessel.

7. The supplemental information disclosure statement filed on 05 January has been considered *in part*.

Information Disclosure Statement

8. The information disclosure statement filed 05 January 2004 fails to comply with 37 CFR 1.98(a)(3) because it does not include a concise explanation of the relevance, as it is presently understood by the individual designated in 37 CFR 1.56(c) most knowledgeable about the content of the information, of each patent/reference listed that is not in the English language. It has been placed in the application file, but the information referred to therein has not been considered. It is noted to Applicant that the document, Kunio Matsunaga et al., is in Japanese. Therefore, an explanation of the relevance of the citation in English is requested by the Examiner. Applicant indicts in the response of 05 January 2004 that an explanation of the relevance of each reference in English is provided. However, no such translation was provided to the Examiner. The basis for this objection is set forth at pg 3 of the previous Office Action (03 July 2004).

Claim Rejections - 35 USC § 112

9. Claim 6 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for treating acute renal failure comprising administering an effective amount of hepatocyte growth factor (HGF) by continuous intravenous administration to suppress blood urea nitrogen (BUN) and creatine levels in a patient suffering from acute renal failure, does not reasonably provide enablement for a method for treating or preventing renal disease which comprises administrating an effective amount of HGF by continuous intravenous administration. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The basis for this rejection is set forth at pg 4-7 of the previous Office Action (03 July 2003).

The claim is directed to a method for treating renal failure, which comprises administering an effective amount of hepatocyte growth factor (HGF) by continuous intravenous administration to a patient suffering from renal failure, thereby treating renal failure in said patient.

Applicant's arguments (05 January 2004), as they pertain to the rejections have been fully considered but are not deemed to be persuasive for the following reasons.

(i) Applicant asserts that the phrase "effective amount" is acceptable since the amount would be readily ascertainable to the skilled artisan. Applicant indicates that dosage amounts are on page 9, lines 4-11 of the specification. Applicant argues that the most recent case law has accepted the phrase "an effective amount" even in the absence of a function to be achieved (*Ex parte Skuballa*, 12 USPQ2d 1570 (Bd. Pat. App. & Inter. 1989). Applicant states that the Board

held that a claim which recited "effective amount of a compound of claim 1" without stating the function to be achieved was definite, particularly when read in light of the supporting disclosure which provided guidelines as to the intend utilities and how the uses could be affected. Applicant argues that the specification of the instant application discloses guidelines for dosage and the intended utilities of HGF.

Applicant's arguments have been fully considered but are not found to be persuasive. The specification of the instant application teaches that continuous intravenous administration of HGF suppresses BUN and creatine levels (pg 12, lines 24-25; pg 15; Figure 4) as well as increases survival rate and platelet counts (pg 17-18; Figure 13). However, there is little or no guidance in the specification to indicate that administration of HGF to patients suffering from renal failure has all possible effects, such as nutritional effects. Undue experimentation would be required of the skilled artisan to determine all possible functions that HGF has after administration to a subject for the treatment of renal failure. In other words, what action or effect does HGF have that allows it to treat renal failure? Also, one skilled in the art would not be able to predict all possible effects that HGF has *in vivo* after it is administered to a patient suffering from renal failure.

Furthermore, the fact patterns of the case cited by the Applicant and of the instant rejection are significantly different, and the court decisions are not binding with regard to the instant rejections. First, the claims of the board decision were rejected on the grounds of being indefinite for the recitation of "effective amount". The claims of the instant application are not only rejected under 35 U.S.C. § 112, second paragraph (see below), but also 35 U.S.C. § 112, first paragraph (enablement). Additionally, the method claim in *Ex parte Skuballa* (claim 20)

recites a method of inhibiting gastric acid secretion or for cytoprotection in a patient comprising administering an effective amount of a compound of claim 1 to the patient. The Board indicates that this claim sets forth the function or functions to be achieved by administering the compound to the patient and is not indefinite. However, claim 6 of the instant application does not recite a function to be achieved, other than treating renal failure.

Proper analysis of the Wands factors was provided in the previous Office Action. Due to the large quantity of experimentation necessary to determine what effect an "effective amount" of HGF has, the lack of direction/guidance presented in the specification regarding the same, the absence of working examples directed to the same, the complex nature of the invention, and the unpredictability of all possible effects of HGF after administration to a patient suffering from renal failure, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

10. Claim 7 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The basis for this rejection is set forth at pg 7-10 of the previous Office Action (03 July 2003).

The claim is directed to a method for treating occlusive lesion of blood vessel, which comprises administrating an effective amount of HGF by continuous intravenous administration to a patient suffering from occlusive lesion of blood vessel, thereby treating occlusive lesion of blood vessel.

Applicant's arguments (05 January 2004), as they pertain to the rejections have been fully considered but are not deemed to be persuasive for the following reasons.

(i) Applicant disagrees with the Examiner's interpretation of "occlusive lesion of blood vessel" as being unduly broad. Applicant indicates that evidence is provided showing that continuous administration of HGF is effective for treating occlusive lesion of blood vessels. Applicant states that the data shows the continuous administration of HGF in rabbit hindlimb ischemia model provides for an improved I/N ratio over continuous administration of a control. Applicant asserts that the rabbit hindlimb ischemia model is a disease model for occlusive lesion of blood vessels.

Applicant's arguments have been fully considered but are not found to be persuasive. The phrase "occlusive lesion of blood vessel" in the claim is still interpreted by the Examiner to be broad, in that it encompasses numerous diseases and disorders with occlusive lesion of blood vessel. Specifically, as discussed in the previous Office Action (03 July 2003), the specification even discloses that examples of occlusive lesion of blood vessel include lower limb ischemia, arterial embolism, arterial thrombosis, Buerger's disease, and pulmonary embolism among others (pg 8, lines 23-28). However, the various disorders disclosed in the specification have different pathophysiologies. The Examiner pointed out, for example, the differences between arterial embolism and Buerger's disease (see previous Office Action and Appendices A and B). Undue experimentation would be required of the skilled artisan to continuously administer HGF to individuals with all possible disorders that cause or are associated with occlusive lesion of blood vessel and successfully treat the disorder. One skilled in the art would also not be able to predict from the of the instant specification that HGF would be able to treat all possible disorders

that cause or are associated with occlusive lesion of blood vessel, such as arterial embolism or Buerger's disease, because occlusive lesion of the blood vessel encompasses many diseases and disorders which have different pathophysiologies.

Furthermore, Applicant's argument is not persuasive because the evidence in the example and graph attached as Exhibit 1 must be submitted in the form of a declaration under 37 C.F.R. 1.132. Exhibit 1 is not proper evidence, since it has not been peer-reviewed and its contents have not been attested to under 37 CFR 1.132. Without submission under 37 C.F.R. 1.132 , it is unclear where the data and the bar graph originate from. However, if submitted under 37 C.F.R. 1.132, the results in Exhibit 1 would still not be persuasive. The Exhibit indicates the administration of HGF in a hindlimb ischemia model only, which is not representative of all possible occlusive lesions of blood vessel. As mentioned above, occlusive lesion of the blood vessel encompasses many diseases and disorders which have different pathophysiologies and HGF treatment in a hindlimb ischemia is not predictive of treatment of all these possible occlusive lesion of blood vessel diseases and disorders. Additionally, according to the graph attached to Exhibit 1, there is no significant difference of the I/N ratio between the vehicle group and the HGF group. Therefore, one skilled in the art would not even be able to predict that continuous administration of HGF would treat hindlimb ischemia, let alone all possible diseases and disorders of occlusive lesion of blood vessel.

Additionally, the arguments of counsel cannot take the place of evidence in the record. In the instant case, the Applicant is asserting that the rabbit hindlimb ischemia model is a disease model for occlusive lesion of blood vessels while no data, information, or teaching supports this assertion in the instant Specification {see *In re Schulze*, 346 F.2d 600, 602, 145 USPQ 716, 718

(CCPA 1965); *In re Geisler*, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997) ("An assertion of what seems to follow from common experience is just attorney argument and not the kind of factual evidence that is required to rebut a prima facie case of obviousness.") and MPEP § 716.01(c)}.

(ii) Applicant argues that the phrase "effective amount" is acceptable since the amount would be readily ascertainable to the skilled artisan. Applicant indicates, for example, that the instant specification discloses specific doses for the treatment of renal disease and occlusive lesion of blood vessel (pg 9, lines 4-11). Applicant states that the most recent case law has accepted the phrase "an effective amount" even in the absence of a function to be achieved (Ex parte Skuballa, 12 USPQ2d 1570 (Bd. Pat. App. & Inter. 1989).

Applicant's arguments have been fully considered but are not found to be persuasive. As discussed above, the fact patterns of the case cited by the Applicant and of the instant rejection are significantly different, and the court decisions are not binding with regard to the instant rejections. First, the claims of the board decision were rejected on the grounds of being indefinite for the recitation of "effective amount". The claims of the instant application are not only rejected under 35 U.S.C. § 112, second paragraph (see below), but also 35 U.S.C. § 112, first paragraph (enablement). Additionally, the method claim in *Ex parte Skuballa* (claim 20) recites a method of inhibiting gastric acid secretion or for cytoprotection in a patient comprising administering an effective amount of a compound of claim 1 to the patient. The Board indicates that this claim sets forth the function or functions to be achieved by administering the compound

to the patient and is not indefinite. However, claim 7 of the instant application does not recite a function to be achieved, other than treating occlusive lesion of blood vessel.

Proper analysis of the Wands factors was provided in the previous Office Action. Due to the large quantity of experimentation necessary to treat and prevent all possible diseases and disorders with occlusive lesion of blood vessel by administration of HGF, the lack of direction/guidance presented in the specification regarding the same, the absence of working examples directed to the same, the complex nature of the invention, the state of the art indicating that glycerol is not used as an animal model for MNMS or occlusive lesion of blood vessel, and the unpredictability of the effects of administration of HGF for all possible diseases or disorders with occlusive lesion of blood vessel to all possible subjects (see discussion), undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Claim Rejections - 35 USC § 112

11. Claims 7 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The basis for this rejection is set forth at pg 10-11 of the previous Office Action (03 July 2003).

12. The term "occlusive lesion of blood vessel" in claim 7 is a relative term which renders the claim indefinite. The term "occlusive lesion of blood vessel" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is not

clear what physiological condition this term is referring to. For example, does "occlusive lesion of blood vessel" mean ischemia, necrosis, or blood clots, for example.

Applicant's arguments (05 January 2004), as they pertain to the rejections have been fully considered but are not deemed to be persuasive for the following reasons.

Applicant argues that the phrase "occlusive lesion of blood vessel" is not unduly broad. Applicant asserts that the data presented as Exhibit 1 shows that the method of the present invention is effective for treating occlusive lesion of blood vessels.

Applicant's arguments have been fully considered but are not found to be persuasive. The method claim in *Ex parte Skuballa* (claim 20) recites a method of inhibiting gastric acid secretion or for cytoprotection in a patient comprising administering an effective amount of a compound of claim 1 to the patient. The Board indicates that this claim sets forth the function or functions to be achieved by administering the compound to the patient and is not indefinite. However, claim 7 of the instant application does not recite a function to be achieved, other than treating occlusive lesion of blood vessel. Applicant's argument is also not persuasive because the evidence in the example and graph attached as Exhibit 1 must be submitted in the form of a declaration under 37 C.F.R. 1.132.

Conclusion

No claims are allowable.

It is noted that Applicant requested an interview should there be any outstanding matters that needed to be resolved. However, the issues currently remaining are too complex to be resolved by an interview.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bridget E. Bunner whose telephone number is (571) 272-0881. The examiner can normally be reached on 8:30-4:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (571) 272-0887. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Elizabeth C. Kemmerer

BEB
Art Unit 1647
14 April 2004

ELIZABETH KEMMERER
PRIMARY EXAMINER